

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (canceled)

2. (currently amended) A method for delivery of double-stranded

oligoribonucleotides across the blood-brain or the blood-retina barrier to an organism in need thereof comprising administering parenterally a composition ~~comprising~~ consisting essentially of one or more naked double-stranded oligoribonucleotides (dsRNA) consisting of 21 to 23 nucleotides into a cell, tissue or organism outside the blood-brain or blood-retina barriers, wherein said dsRNA is trafficked across said blood-brain or blood-retina barrier, wherein first and second strands of said dsRNA are complementary to each other.

3. (previously presented) The method of claim 2, wherein said method results in the provision of a test cell, test tissue or test organism, which can be-maintained under conditions allowing the degradation of the corresponding mRNA of one or more of target genes by RNA interference.

4. (previously presented) The method of claim 3 for the identification or validation of the function of a gene, further comprising comparing a resulting phenotype produced in the test cell, test tissue or test organism with that of a suitable control, thus allowing information on the function of the gene to be gained.

5. (previously presented) The method of claim 2, wherein the introduced dsRNA inhibits expression of a target gene that is expressed behind the blood-brain or blood-retina barrier.

6. (previously presented) The method of claim 5, wherein one or more of said target genes encode a cellular mRNA.

7. (previously presented) The method of claim 2, wherein the cells or tissues are cells or tissues of the eye.

8. (previously presented) The method of claim 2, wherein said cells or tissues are cells or tissues of the inner segment of the eye ball.

9. (previously presented) The method of claim 8, wherein said cells are retinal cells.

10. (previously presented) The method of claim 9, wherein said cells are cells of the retinal pigment epithelium (RPE) or neurosensory retina cells.

11. (previously presented) The method of claim 2, wherein one or more of said target genes are predominantly expressed in said cell or tissue.

12. (previously presented) The method of claim 2, wherein the expression of one or more of said target genes is specific for said cell or tissue.

13. (previously presented) The method of claim 2, wherein said dsRNA molecules are selected from the group consisting of 21 and 22 nucleotides in length.

14. (withdrawn-previously presented) The method of claim 2, wherein said dsRNA molecules contain a terminal 3'-hydroxyl group.

15. (withdrawn-previously presented) The method of claim 2, wherein said dsRNA molecules are chemically synthesized.

16. (withdrawn-previously presented) The method of claim 2, wherein said dsRNA molecules represent an analogue of naturally occurring RNA.

17. (withdrawn-previously presented) The method of claim 16, wherein said dsRNA analogues differ from a corresponding naturally occurring RNA by addition, deletion, substitution or modification of one or more nucleotides.

18. (withdrawn-previously presented) The method of claim 2 wherein said dsRNA molecules inhibit target genes by posttranscriptional silencing.

19. (previously presented) The method of claim 2, wherein said dsRNA molecules are encoded by a vector.

20. (previously presented) The method of claim 19, wherein the expression of said dsRNA is under control of a cell or tissue specific promoter.

21-23. (canceled)

24. (previously presented) The method of claim 2, wherein the dsRNA molecules are delivered continuously to the target cells or target tissues over a defined period of time after application.

25. (canceled)

26. (previously presented) The method of claim 2, wherein said composition is introduced by a method selected from the group consisting of iontophoresis, retrobulbar application, systemic application, topical application on the eye, or a combination of any thereof.

27. (previously presented) The method of claim 2, wherein the cells, tissues or organism is a vertebrate.

28. (previously presented) The method of claim 2, wherein the cells, tissues or organism is mammalian.

29.-30. (canceled)

31. (previously presented) The method of claim 2, wherein the cells, tissues or organism are human.

32.-45. (canceled)

46. (previously presented) The use of the method of claim 4, in drug discovery, target gene isolation, or drug validation.

47. (canceled)

48. (previously presented) The method of claim 2, wherein the dsRNA contains two symmetrical 3' overhangs of two nucleotides in length.

49. (previously presented) The method of claim 48, wherein the overhangs comprise 2'-deoxy-thymidine.

50. (previously presented) The method of claim 5, wherein the inhibition of target gene expression treats a retinal disease.

51. (previously presented) The method of claim 5, wherein the inhibition of target gene expression treats a degenerative retinal disease.

52. (previously presented) The method of claim 51, wherein the degenerative retinal disease is selected from the group consisting of: primary detachment of the retina, retinoblastoma, retinal astrocytoma, angiomas retinae, Coats disease, Eales disease, retinopathia centralis serosa, ocular albinism, retinitis pigmentosa, retinitis punctata albescens, Usher's syndrome, Leber's congenital amaurosis, cone dystrophy, vitelliforme macular degeneration, juvenile retinoschisis, North Carolina macular dystrophy, Sorsby fundus-dystrophy, Doyme's honeycombs, retinal dystrophy, Morbus Stargardt, Wagner's vitreoretinal degeneration and age-dependent macular degeneration.

53. (previously presented) The method of claim 51, wherein the degenerative retinal disease is age-dependent macular degeneration.

54. (canceled)

55. (withdrawn-previously presented) The method of claim 22, wherein the coat protein is derived from a virus selected from the group consisting of a cytomegalovirus, an adeno-associated virus and an adenovirus.

56. (previously presented) The method of claim 2, wherein said composition is administered intravenously.

57. (previously presented) A method for delivery of double-stranded oligoribonucleotides across the blood-brain or the blood-retina barrier to an organism in need thereof comprising administering parenterally a composition consisting essentially of saline and one or more naked double-stranded oligoribonucleotides (dsRNA) consisting of 21 to 23 nucleotides into a cell, tissue or organism outside the blood-brain or blood-retina barriers, wherein said dsRNA is trafficked across said blood-brain or blood-retina barrier,

wherein first and second strands of said dsRNA are complementary to each other.

58. (previously presented) The method of claim 57, wherein said composition consists of saline and one or more naked double-stranded oligoribonucleotides (dsRNA) consisting of 21 to 23 nucleotides.